

INTRAVENOUS MESENCHYMAL STEM CELLS ADMINISTRATION INDUCES SURVIVAL AND SYMPTOM AMELIORATION IN MUTANT SOD1 G93A MICE.

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Amyotrophic lateral sclerosis (ALS) is a chronic neuromuscular disorder, clinically characterized by muscle wasting, weakness and spasticity reflecting a progressive degeneration of upper and lower motor neurons. To date any treatments hardly prolong survival in ALS patients of some extent. Development of more effective neuroprotective therapies is impeded by lack of understanding of the mechanisms of neuronal death and how the disease propagates. Mesenchymal stem cells (MSC), a subset of adult stem cells derived from the bone marrow stroma, have generated much enthusiasm as possible cell source for tissue repair including the nervous system. Recent studies have shown different MSC roles as to modulate immune responses and to exert an anti-apoptotic effect on different cells including neurons. In addition, MSC can migrate into the central nervous system when i.v. injected. We studied here the effects of MSC administration in mice expressing mutant human super oxide dismutase (SOD1) with a G93A substitution [SOD1(+)/G93A(+)], a transgenic animal model of ALS. Mesenchymal cells (10^6 cells/animal, i.v.) were injected at day 90, well after the onset of the first disease symptoms, that can be recorded at about day 60. Saline injected SOD1(+)/G93A(+) were used as controls. Control mice survived about 120 days while the MSC-treated mice exhibited a statistically significant prolonged survival time compared to saline injected controls. Such effect was associated with a significant amelioration in the performance of behavioral motor tests in the MSC-treated animals. Studying neurotransmitter release, we have found that glutamate exocytosis is enhanced in the spinal cord of SOD1(+)-G93A(+) mice, respect to controls. Interestingly, MSC treatment almost abolished this extra-release of the excitatory amino acid. Upon i.v. injection, a few luciferase-labeled MSCs were detected inside the mice spinal cord. Amelioration of some histological parameters was observed irrespective neural trans-differentiation. We can conclude that the treatment with MSC may be considered as an appealing therapeutic opportunity for ALS although the effect does not seem to rely on tissue repair.